Transferable cell-secreted extracellular matrices enhance osteogenic differentiation.

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Authors: M L Decaris, A Mojadedi, A Bhat, J K Leach

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Public Summary:
The coating of synthetic biomaterials with cell-derived decellularized extracellular matrices (DMs) represents a promising approach to confer bioactivity to otherwise inert materials and direct cell fate of host or transplanted cells. These coatings are typically deposited on biomaterials by culturing matrix-depositing cells for a sufficient duration on the target, followed by decellularization of the substrate. We hypothesized that DMs created in monolayer culture could be collected and then transferred to a secondary substrate while retaining their instructive potential. Transferred decellularized matrices (tDMs) were created by culturing human mesenchymal stem cells (hMSCs) on tissue culture plastic (TCP) under a controlled microenvironment to deposit a highly osteogenic DM, followed by collection, mechanical homogenization and transfer to a secondary culture surface. We then investigated its capacity to accelerate naïve hMSC osteogenic differentiation by quantifying gene expression, intracellular alkaline phosphatase production, and calcium deposition when cultured on DMs or tDMs. All markers were significantly higher in hMSCs seeded on DMs or tDMs compared to cells on TCP. The osteogenic response of naïve hMSCs to tDMs was dose dependent. We observed a reduction in ERK phosphorylation in hMSCs, as well as a possible role of the cell surface integrin α2β1, when probing the mode of efficacy for tDMs. This study represents a proof-of-principle that cell-derived matrix coatings can be deposited and effectively transferred while retaining the ability to instruct cell phenotype, thus offering a novel approach toward the development of hybrid biomaterials that mimic the complex interactions between cells and the extracellular matrix.

Scientific Abstract:
The coating of synthetic biomaterials with cell-derived decellularized extracellular matrices (DMs) represents a promising approach to confer bioactivity to otherwise inert materials and direct cell fate of host or transplanted cells. These coatings are typically deposited on biomaterials by culturing matrix-depositing cells for a sufficient duration on the target, followed by decellularization of the substrate. We hypothesized that DMs created in monolayer culture could be collected and then transferred to a secondary substrate while retaining their instructive potential. Transferred decellularized matrices (tDMs) were created by culturing human mesenchymal stem cells (hMSCs) on tissue culture plastic (TCP) under a controlled microenvironment to deposit a highly osteogenic DM, followed by collection, mechanical homogenization and transfer to a secondary culture surface. We then investigated its capacity to accelerate naive hMSC osteogenic differentiation by quantifying gene expression, intracellular alkaline phosphatase production, and calcium deposition when cultured on DMs or tDMs. All markers were significantly higher in hMSCs seeded on DMs or tDMs compared to cells on TCP. The osteogenic response of naive hMSCs to tDMs was dose dependent. We observed a reduction in ERK phosphorylation in hMSCs, as well as a possible role of the cell surface integrin alpha(2)beta(1), when probing the mode of efficacy for tDMs. This study represents a proof-of-principle that cell-derived matrix coatings can be deposited and effectively transferred while retaining the ability to instruct cell phenotype, thus offering a novel approach toward the development of hybrid biomaterials that mimic the complex interactions between cells and the extracellular matrix.